WHAT IS CLAIMED IS:

Sub A1

1. An isolated nucleic acid coding for an HPC2 polypeptide, said polypeptide comprisingg the amino acid sequence set forth in SEQ ID NO:2 or a modified form which is functionally equivalent.

2. The isolated nucleic acid of claim 1 wherein said DNA has the nucleotide sequence (a) set forth in SEQ ID NO:1, (b) its complement, (c) a corresponding RNA or (d) a nucleotide sequence which hybridizes under stringent conditions to the nucleotide sequence of (a), (b) or (c).

3. The isolated nucleic acid of claim 1 wherein said DNA has the nucleotide sequence set forth in SEQ ID NO:3, SEQ ID NO:28, or complements thereof.

4. The isolated nucleic acid of claim 1 which is a DNA comprising an allelic variant of the nucleotide sequence set forth in SEQ ID NO:1, its complement or a corresponding RNA.

5. The isolated nucleic acid of claim 1 coding for a mutated form of the HPC2 polypeptide set forth in SEQ ID NO:2.

6. The isolated nucleic acid of claim 5 which is a DNA comprising a mutated form of the nucleotide sequence set forth in SEQ ID NO:1, its complement or a corresponding RNA.

7. The isolated nucleic acid of claim 6 wherein the mutation is selected from the group consisting of a deletion mutation, a nonsense mutation, an insertion mutation, a frameshift mutation and a missense mutation.

8. An isolated nucleic acid having a nucleotide sequence selected from the group consisting of (a) SEQ ID NOs:4-27, (b) complements thereof, (c) RNAs corresponding thereto and (d) nucleic acids which hybridize under stringent conditions to the nucleotide sequences of (a), (b) or (c).

9. An isolated nucleic acid having at least 15 contiguous nucleotides of a nucleic acid as claimed in claim 1 wherein the nucleic acid sequence suitable for use as a hybridization probe to detect in a sample (i) a DNA having a nucleotide sequence selected from the nucleotide sequence set forth in SEQ ID NO:1, allelic variants thereof and mutated forms thereof, (ii) an RNA corresponding to said DNA or (iii) a nucleotide sequence which hybridizes under stringent conditions to the nucleotide sequence of (i) or (ii).

Sub A2

10. A set of nucleic acid probes for use in a microchip assay wherein each of said nucleic acid probes comprises at least 8 contiguous nucleotides of a nucleic acid as claimed in claim 1 and said set encompasses part or all of said nucleic acid.

11. A vector which comprises an isolated nucleic acid as claimed in claim 1.

Sub A3

12. An expression vector which comprises an isolated nucleic acid of claim 1 wherein the coding sequence for the HPC2 polypeptide or modified form thereof is operably linked to suitable control sequences capable of directing expression of said coding sequence in host cells for said vector.

13. Host cells transformed with a vector as claimed in claim 11.

Sub A4

14. A method of producing a polypeptide which is the HPC2 polypeptide of claim 1 which comprises (i) culturing the host cells containing an expression vector encoding said polypeptide under conditions suitable for the production of said HPC2 polypeptide and (ii) recovering said polypeptide.

15. A method as claimed in claim 14 which further comprises labeling the recovered polypeptide.

16. A preparation of human HPC2 polypeptide substantially free of other human proteins, said polypeptide having the amino acid sequence set forth in SEQ ID NO:2.

17. A preparation of human HPC2 polypeptide substantially free of other human proteins, the amino acid sequence of said polypeptide having substantial sequence homology with

the wild-type HPC2 polypeptide having the amino acid sequence set forth in SEQ ID NO:2, and said polypeptide having substantially similar function as the wild-type HPC2 polypeptide.

18. A preparation of a polypeptide substantially free of other proteins, said polypeptide being a mutated human HPC2 polypeptide obtainable by expression of a mutated form of the nucleic acid sequence set forth in SEQ ID NO:2.

19. A preparation as claimed in claim 16 wherein said polypeptide is labeled.

20. An antibody capable of specifically binding one or more polypeptides as claimed in claim 16.

21. An antigenic fragment of a polypeptide as defined in claim 16 suitable for use as an immunogen to obtain an antibody.

22. A polypeptide as defined in claim 16 in the form of a fusion protein.

23. Use of a polypeptide as defined in claim 16 as an immunogen for antibody production.

24. A use as claimed in claim 23 wherein one or more antibodies products are subsequently labeled or bound to a solid support.

Sub A5

25. A pair of single-stranded oligonucleotide primers for determination of a nucleotide sequence of a *HPC2* gene by a nucleic acid amplification reaction, the sequence of said primers being derived from genomic clones for *HPC2*, and the use of said primers in a nucleic acid amplification reaction resulting in the synthesis of DNA or RNA corresponding to all or part of the sequence of the *HPC2* gene.

26. A pair of primers as claimed in claim 25 for determination of all or part of the sequence of the *HPC2* gene having the nucleotide sequence set forth in SEQ ID NO:1, allelic variant or a mutated form thereof.

27. A method for identifying a mutant *HPC2* nucleotide sequence in a suspected mutant *HPC2* allele which comprises comparing the nucleotide sequence of the suspected mutant *HPC2* allele with a wild-type *HPC2* nucleotide sequence, wherein a difference between the suspected mutant and the wild-type sequence identifies a mutant *HPC2* nucleotide sequence.

28. A method for detecting an alteration in *HPC2* wherein said alteration is associated with cancer in a human, wherein if said alteration is in germline it is associated with predisposition to said cancer and if said alteration is in somatic tissue it indicates that said somatic tissue is cancerous, wherein said method comprises analyzing an *HPC2* gene or an *HPC2* gene expression product from a tissue of said human.

29. A method as claimed in claim 28 wherein the sequence of the *HPC2* gene in said sample is compared with the sequence of one or more wild-type *HPC2* gene sequences selected from the sequence set forth in SEQ ID NO:1 and wild-type allelic variants thereof.

30. The method of claim 28 wherein said expression product is selected from the group consisting of mRNA of the *HPC2* gene and a HPC2 polypeptide encoded by the *HPC2* gene.

31. The method of claim 28 wherein one or more of the following procedures is carried out:

(a) observing shifts in electrophoretic mobility of single-stranded DNA from said sample on non-denaturing polyacrylamide gels;

(b) hybridizing a *HPC2* gene probe to genomic DNA isolated from said sample under conditions suitable for hybridization of said probe to said gene;

(c) determining hybridization of an allele-specific probe to genomic DNA from said sample;

(d) amplifying all or part of the *HPC2* gene from said sample to produce an amplified sequence and sequencing the amplified sequence;

(e) determining by nucleic acid amplification the presence of a specific *HPC2* mutant allele in said sample;

(f) molecularly cloning all or part of the *HPC2* gene from said sample to produce a cloned sequence and sequencing the cloned sequence;

(g) determining whether there is a mismatch between molecules (1) *HPC2* gene genomic DNA or *HPC2* mRNA isolated from said sample, and (2) a nucleic acid probe complementary to the human wild-type *HPC2* gene DNA, when molecules (1) and (2) are hybridized to each other to form a duplex;

(h) amplification of *HPC2* gene sequences in said sample and hybridization of the amplified sequences to nucleic acid probes which comprise wild-type *HPC2* gene sequences;

(i) amplification of *HPC2* gene sequences in said tissue and hybridization of the amplified sequences to nucleic acid probes which comprise mutant *HPC2* gene sequences;

(j) screening for a deletion mutation;

(k) screening for a point mutation;

(l) screening for an insertion mutation;

(m) determining *in situ* hybridization of the *HPC2* gene in said sample with one or more nucleic acid probes which comprise the *HPC2* gene sequence or a mutant *HPC2* gene sequence;

(n) immunoblotting;

(o) immunocytochemistry;

(p) assaying for binding interactions between HPC2 protein isolated from said tissue and a binding partner capable of specifically binding the polypeptide expression product of a *HPC2* mutant allele and/or a binding partner for the HPC2 polypeptide having the amino acid sequence set forth in SEQ ID NO:3; and

(q) assaying for the inhibition of biochemical activity of said binding partner.

32. A non-human animal which carries an altered *HPC2* allele in its genome.

33. A non-human animal in which its native *HPC2* alleles have been replaced by *HPC2* alleles from a second animal.

34. A non-human animal in which its native *HPC2* alleles have been disrupted or deleted.

35. A non-human animal in which one or both of its native *HPC2* alleles have been (a) modified to contain a DNA system to conditionally knockout said alleles or (b) have

been replaced by *HPC2* alleles from a second animal modified to contain a DNA system to conditionally knockout said alleles.

36. A cell line isolated from the non-human animal of claim 32.

37. An isolated mutant HPC2 which cannot form a complex with a wild-type binding partner with which wild-type HPC2 does form a complex.

38. An isolated protein complex comprising HPC2 and its binding partner.

39. A protein complex comprising a fragment of HPC2 and a fragment of its binding partner.

40. An isolated antibody immunoreactive with the protein complex of claim 38.

41. The antibody of claim 40 wherein said antibody is not immunoreactive with either pure HPC2 or pure HPC2-binding partner.

42. The antibody of claim 40 wherein said antibody is a monoclonal antibody.

43. A method for supplying a wild-type *HPC2* gene function or a *HPC2* function substantially similar to said wild-type function to a cell which has lost said gene function or has altered gene function by virtue of a mutation in said *HPC2* gene, wherein said method comprises introducing into the cell a nucleic acid which restores an *HPC2* function in said cell, said nucleic acid selected from the group consisting of a wild-type *HPC2* gene nucleic acid or a nucleic acid substantially homologous to said wild-type *HPC2* gene nucleic acid, such that said nucleic acid is expressed in said cell.

44. The method of claim 43 wherein said nucleic acid is a portion of wild-type HPC2 gene, said portion encoding a part of said wild-type gene polypeptide which is biologically functional.

45. A method for supplying a wild-type *HPC2* gene function or a HPC2 function substantially similar to wild-type to a cell which has lost said gene function or has altered

gene function by virtue of a mutation in said *HPC2* gene, wherein said method comprises introducing into said cell a molecule which restores an *HPC2* function in said cell, said molecule selected from the group consisting of all or a part of a wild-type HPC2 polypeptide which is biologically functional, a polypeptide substantially homologous to said wild-type HPC2 polypeptide and a molecule which mimics the function of said wild-type HPC2 polypeptide.

46. A method for diagnosing a predisposition for cancer in a human wherein said method comprises assaying for the ability of HPC2 or a fragment of HPC2 from said human to form a complex with a binding partner to which wild-type HPC2 binds wherein an inability to form said complex is indicative of a predisposition to cancer.

47. The method of claim 46 wherein said assay comprises a yeast two-hybrid assay.

48. The method of claim 46 wherein said assay comprises measuring *in vitro* a complex formed by mixing said binding partner and HPC2 purified from said human.

49. The method of claim 46 wherein said assay comprises measuring *in vitro* a complex formed by mixing HPC2 and said binding partner purified from said human.

50. The method of claim 46 wherein said complex is measured by binding with an antibody specific for a HPC2-said binding partner complex.

51. The method of claim 46 wherein said assay comprises mixing an antibody specific for a HPC2-said binding partner complex with a tissue extract from said person, wherein the lack of formation of a HPC2-said binding partner-antibody complex between said antibody and said tissue extract is indicative of a predisposition to cancer.

52. A method for determining whether a mutation in *HPC2* is predispositive for cancer, wherein said method comprises binding a HPC2 with said mutation to a binding partner to which wild-type HPC2 binds and determining whether a complex forms, wherein the lack of a complex indicates said mutation is predispositive.

53. A method of screening for drug candidates useful in treating a cancer resulting from a mutation in *HPC2*, wherein said method involves mixing a mutant HPC2 with a wild-type binding partner to which wild-type HPC2 binds, in both the presence of a drug and the absence of said drug and measuring the amount of binding of said mutant HPC2 with said wild-type binding partner, wherein if the amount of said binding is greater in the presence of said drug than in the absence of said drug then said drug is a drug candidate for treating said cancer.

54. The method of claim 53 wherein said mutant HPC2 is a fusion protein and/or said wild-type protein is a fusion protein.

55. A method of screening for drug candidates useful in treating a cancer resulting from a mutation in *HPC2*, wherein said method involves mixing a mutant HPC2 with a wild-type binding partner, to which wild-type HPC2 binds, in both the presence of a drug and the absence of said drug and measuring the amount of binding of said mutant HPC2 with said wild-type binding partner, wherein if the amount of said binding is less in the presence of said drug than in the absence of said drug then said drug is a drug candidate for treating said cancer.

56. The method of claim 55 wherein said wild-type HPC2 is a fusion protein and/or said wild-type binding partner is a fusion protein.

57. A method of screening for drug candidates useful in treating a cancer resulting from a mutation in *HPC2*, wherein said method comprises treating an animal which is homozygous for *HPC2* containing said mutation with a drug wherein if said animal does not develop cancer said drug is a drug candidate for treating said cancer.

58. A method of screening for drug candidates useful in treating a cancer resulting from a mutation in *HPC2*, wherein said method comprises treating an animal which has a tumor and which is homozygous for *HPC2* containing said mutation with a drug wherein if said tumor regresses said drug is a drug candidate for treating said cancer.

59. The method of claim 57 wherein said animal is transgenic for *HPC2* with said mutation.

60. A method of screening for drug candidates useful in treating a cancer resulting from a mutation in *HPC2*, wherein said method comprises the steps of:

(a) growing a cell culture of cells which are homozygous for *HPC2* containing said mutation in the presence of a drug,

(b) growing a cell culture of cells which contain a wild-type *HPC2* gene, and

(c) growing a cell culture of cells which are homozygous for *HPC2* containing said mutation in the absence of said drug,

wherein if the cells in step (a) behave more like the cells in step (b) than like the cells in step (c) then said drug is a drug candidate for treating said cancer.